Human Pathology: Case Reports 8 (2017) 20–23

Contents lists available at ScienceDirect

Human Pathology: Case Reports

journal homepage: http://www.humanpathologycasereports.com

Case Report

Perforated gastric metastasis of Merkel cell carcinoma: Case report and review of the literature☆

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ARTICLE INFO

Article history:
Received 25 August 2016
Received in revised form 5 January 2017
Accepted 12 January 2017

Keywords:
Merkel cell carcinoma
Gastric metastasis
Perforation
Merkel cell polyomavirus
Immunohistochemistry

ABSTRACT

A 53 year-old Vietnamese male presented with a complaint of a left buttock mass which had grown to 8.0 cm during the past three years. A CT scan revealed the gluteal lesion and a large mass of the stomach. A biopsy of the gluteal skin lesion was diagnosed as a high grade neuroendocrine carcinoma consistent with Merkel cell carcinoma. Tumor cells in the gastric biopsy showed the same morphology and immunophenotype as seen in the skin biopsy, and expressed synaptophysin, chromogranin, CD56, and cytokeratin (CK) 20 with perinuclear dot-like staining. The diagnosis of gastric metastasis of Merkel cell carcinoma was further confirmed by immunohistochemistry for Merkel cell polyomavirus (MCPyV). The patient underwent one cycle of chemotherapy until he presented with a perforation of the gastric lesion. Surgical resection was performed, with subsequent pathologic analysis of the stomach lesion interpreted as metastatic Merkel cell carcinoma. Herein we describe the first case of perforated gastric metastasis of Merkel cell carcinoma. Histopathological diagnosis of perforated gastric metastasis of Merkel cell carcinoma was established by characteristic immunostains for CK20 and MCPyV in addition to the positive stains for neuroendocrine markers (synaptophysin, chromogranin and CD56).

1. Introduction

Merkel cells were first described by a German pathologist, Friedrich Sigmund Merkel, as clear oval cells in the basal layer of skin, hair follicles, and oral mucosa [1]. These cells are considered to originate from neural crest cells [2]. Merkel cell carcinoma (MCC), the term initially coined by De Wolf-Peeters et al. in 1980 [3], is believed to derive from Merkel cells, since they both possess dense core neuroendocrine granules, neurofilament, and CK20 expression [2,4]. According to the data from Surveillance, Epidemiology and End Results, there has been a three-fold increase in MCC cases [5], with a predicted 1500 cases per year in the United States [6]. MCC has a predisposition for older, fair-skinned and immunocompromised individuals [7,8]. The mean age of diagnosis is approximately 75 years, with 95% of reported cases occurring in Caucasian patients [7,8]. MCC typically occurs on sun-exposed areas with roughly 50% of cases occurring on the head and neck, and 40% on the extremities [7,8]. MCC has a high local recurrence rate, and the clinical outcome is dismal with 3-year overall survival of 31% [9]. The most common sites of distant metastasis include distant lymph nodes, distant skin, lung, liver, brain, and bone [9,10,11]. Metastasis of MCC to the stomach is extremely rare. To our knowledge, a gastric metastasis of MCC has been reported in only nine previous English-language case reports (Table 1) [12–20].

In 2008, a novel polyomavirus, named Merkel cell carcinoma polyomavirus (MCPyV), was found to be associated with the development of MCC [21]. MCPyV expression has been found in 75% of MCC by immunohistochemistry and 88% of MCC by quantitative polymerase chain reaction [22].

Herein we report a patient with perforated gastric metastasis of Merkel cell carcinoma, which was diagnosed based on histopathological evaluation of the primary and mestastatic tumors in combination with immunohistochemical stains.

2. Case report

A 53 year old Vietnamese male with a medical history of half-pack/day cigarette smoking, gastroesophageal reflux disease, and no known history of significant sun-exposure presented to the emergency department with a complaint of left buttock pain. The patient lived the majority of his life in Vietnam. He first noticed the presence of a small 'bead-like' lesion on the left buttock 3 years ago. The lesion had been growing slowly until 3–4 months prior to his presentation at the emergency department when it began to grow rapidly and ulcerate. Irrigation and drainage, followed by antibiotic therapy, was performed first at another

☆ This case was presented at the 2016 ASCP (American Society of Clinical Pathology) annual meeting, Las Vegas, USA, September 14–16, 2016.

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http://dx.doi.org/10.1016/j.ehpc.2017.01.001

Table 1
Reported Cases of Gastric Metastasis of MCC.

Reference	Age	Gender	Ethnicity	Primary Site	Duration[a]	Outcome	Duration[b]
[7]	79 y	F	Unknown	Groin	4 y	Dead	4 mo
[8]	46 y	M	Caucasian	Preauricular	8 mo	Unknown	Unknown
[9]	60 y	M	Hispanic	Groin	4 mo	Unknown	Unknown
[10]	92 y	M	Caucasian	Arm	15 mo	Dead	5 wk
[11]	67 y	M	Unknown	Buttock	11 mo	Unknown	Unknown
[12]	81 y	M	Unknown	Finger	12 mo	Dead	3 wk
[13]	62 y	M	Unknown	Neck	6 y	Dead	1 m
[14]	80 y	M	Unknown	Arm	2 y	Dead	Unknown
[15]	72 y	F	Unknown	Groin	2 y	Alive	24 mo
This case	53 y	M	Asian	Buttock	3 y	Alive	15 mo

y: years.
mo: months.
F: female.
M: male.
[a] The duration between initial diagnosis and metastasis.
[b] The duration between metastatic diagnosis and death.

hospital without improvement. Upon presentation to the emergency department, the gluteal skin lesion had grown to 8 cm. A CT scan was performed to evaluate the gluteal skin lesion. Incidental findings of this study included a large mass-like thickening of the greater curvature of the stomach. Biopsy was taken from the gluteal lesion (Fig. 1). An esophagogastroduodenoscopy (EGD) was also performed to further evaluate the gastric mass. EGD showed a friable, ulcerated mass with heaped edges spanning 6 cm. Biopsy of this lesion was taken with additional random gastric biopsies (Fig. 2). Other clinical findings during this patient's workup included hepatitis C viral infection, cirrhosis, and a cystic lesion in the pancreatic head radiographically interpreted as an intraductal papillary mucinous neoplasm. Both the gluteal skin lesion (Fig. 1) and the gastric lesion (Fig. 2) demonstrated high grade small round cell neoplasm with neuroendocrine features composed of sheaths of small round tumor cells with hyperchromatic nuclei and scant cytoplasm. The tumor cells in the gluteal skin lesion and the gastric lesion showed the same immunophenotype including positive expression of pan-cytokeratin, cytokeratin 20 (CK20) with dot-like staining pattern, synaptophysin, chromogranin and CD56, and negative expression of TTF-1, S-100, and Melan-A. To confirm the diagnosis of Merkel cell carcinoma, the tissue was sent for CM2B4 immunohistochemistry, which is specific for the large tumor antigen in the polyomavirus positive Merkel cell carcinoma. The immunohistochemistry was performed at Memorial Sloan Kettering Cancer Center, and was interpreted as positive (Fig. 3), confirming the diagnosis of metastatic Merkel cell carcinoma from the primary gluteal skin lesion. The background stomach showed chronic active gastritis with positive Helicobacter pylori infection confirmed by immunohistochemistry.

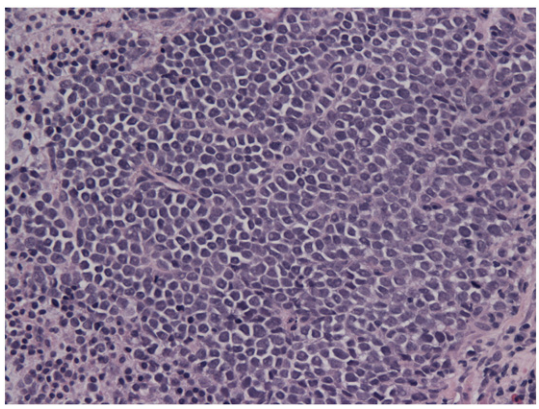

Fig. 1. The gluteal skin biopsy shows high grade small round cell neoplasm with neuroendocrine features composed of sheaths of small round cells with hyperchromatic nuclei and scant cytoplasm (H&E. ×200).

The patient underwent one cycle of chemotherapy with cisplatin and etoposide. Shortly afterward he presented with sharp abdominal pain, and was found to have a perforation of the gastric lesion. Emergency wedge gastrectomy was performed with subsequent analysis of the surgical specimen. The surgical specimen consisted of a single gastric wedge resection measuring 12.5 × 7.5 × 3.3 cm. A perforated mass lesion with heaped edges measuring 8.5 cm was noted in the center of resected specimen. Sections of the surgical specimen demonstrated a perforated tumor (Fig. 4) composed of high grade small round cell neoplasm with neuroendocrine features (Fig. 5). Immunohistochemical studies showed positive expression of CK 20 with dot-like staining pattern (Fig. 6), synaptophysin, chromogranin with dot-like staining pattern (Fig. 7) and CD56. This was the same morphology and immunophenotype as seen in the skin and gastric biopsies, confirming the diagnosis of perforated gastric metastasis of Merkel cell carcinoma.

A follow up CT scan at two months after the surgery showed a 6.7 cm oropharyngeal mass extending into the larynx. The biopsy of the oropharyngeal mass was positive for metastatic MCC. The patient restarted and completed six cycles of chemotherapy with carboplatin and etoposide, and also underwent radiation therapy to left buttock lesion. At the time of this writing, the patient is alive and disease-free at 18 months after initial presentation of left buttock pain. All biopsy procedures, surgery, chemotherapy, and radiation therapy were performed in the United States.

3. Discussion

Merkel cell carcinoma (MCC) is a rare primary cutaneous neuroendocrine carcinoma composed of malignant small round cells with

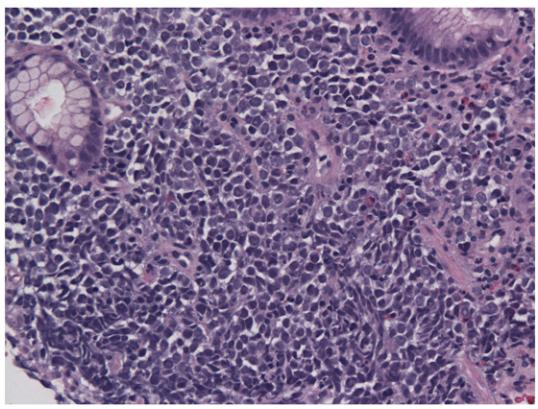

Fig. 2. The gastric biopsy shows high grade small round cell neoplasm with neuroendocrine features. This is the same morphology as seen in the skin biopsy (H&E. ×200).